Alcohol and Drug Use— Is There a 'Safe' Amount?

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All human endeavors are associated with quantifiable risks. Knowledge of the risk is essential for personal health maintenance. Nontherapeutic use of psychoactive drugs poses an important danger to individual persons and society. What are the quantitative estimates of these risks? Are they acceptable?

Because the basic mechanism of the toxic effect of alcohol or other drugs is unknown, deciding on acceptable risks is difficult. Based on current information, the recreational abuse of inhalants, hallucinogens, stimulants, narcotics and sedative-hypnotic drugs poses unacceptable individual and societal risks. Groups at special risk should not consume alcohol or any drug unless they are under medical supervision. The threshold for increased morbidity from the regular use of alcohol in adults is in the range of three to five drinks per day; this rises sharply after six drinks per day. The apparent "safe" level of alcohol consumption appears to be one to two drinks per day. Further basic studies are required to refine these risk estimates.

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Alcohol- and drug-related illnesses are major public health problems in modern society. With insufficient dollars for health care it is certain that individual persons and society will more closely examine ways to maintain personal health. Alcohol and other drugs are widely used for their mind-altering effects. The "use" or "abuse" of mind-altering agents evokes strong feelings. Conflicts of personal freedom and public danger pose difficult political and philosophical questions, especially when prolonged low-dose consumption for recreational purposes is considered. Complex variables of dose, genetic factors, prior drug exposure and drug interactions all present difficult scientific questions. Do we focus on the drug, on protecting society or on protecting the person at risk? Can we easily distinguish voluntary from involuntary risks? Much has been learned recently concerning broad guidelines for approaching these problems. Important decisions for personal health maintenance may require changes in public and private policy. Perhaps the best approach is to ask, is there a "safe" level of alcohol and drug consumption? If a dose of alcohol or a drug is consumed at a given time and place, are there "acceptable" risks? If this risk can be quantitated and scientifically studied, we can more rationally approach the problem. As with all such risk assessments, we are required to make important decisions with incomplete information.

Scope of the Problem

Drug and alcohol consumption are often viewed together. It is useful to approach the data on alcohol first, as alcohol forms the background for many other drug issues. The consumption of alcohol has increased by more than 30% in the past 20 years. Currently more than 200,000 Americans die annually from alcohol-related deaths and as many as a third of adult patients in hospitals have problems related to alcohol abuse. About 20% of our total national expenditure for health care is for problems related to alcohol abuse. Two thirds of all incidents of domestic violence involve the use of alcohol and a third of the cases of child abuse are alcohol related. About 50% of traffic fatalities, fire deaths, rapes and suicides are thought to involve alcohol.[1] One out of every two Americans will be in an alcohol-related traffic accident during his or her lifetime and, on an average weekend night, one out of every ten drivers on the road is under the influence of alcohol.[2]

Another way to estimate the scope of the problem with alcohol is to examine the total amount of alcohol consumed by a given group. It is possible to estimate alcohol consumption

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ABBREVIATIONS USED IN TEXT
CT = computed tomography
HBsAg = hepatitis B surface antigen
HDL = high-density lipoprotein

based on sales taxes collected at the federal, state and local levels. Of the tax dollars collected in the year 1982-1983, the California State Department of Alcohol and Drugs reports that more than $1 billion was collected from alcoholic beverages. The total consumption in California per capita is about 40 gal of alcohol per year: 31 gal of beer, 5.9 gal of wine and 2.8 gal of distilled spirits. This consumption is about 25% greater than the national average. Not only do Californians drink more per capita than the national average but a greater proportion of Californians drink. Of Californians, about 78% drink alcoholic beverages during the year, with 22% abstaining. Nationwide, about 67% drink and 33% abstain.

What is the risk of 40 gal of alcoholic beverage consumed per year? Theoretically, it is possible to epidemiologically study the health consequences of this consumption. Unfortunately, consumption is not evenly distributed. Although it is difficult to quantitate, most reasonable estimates are that between 10% and 15% of the population consume about 75% to 80% of the alcoholic beverages. It is evident from even these rough estimates that a relatively small percentage of the population consumes most of the alcohol.

Another way to estimate the problem is to recognize that alcoholic beverages are freely available as an over-the-counter drug in 60,000 outlets in California. Alcohol is relatively inexpensive, as its price increases at only 70% of the Consumer Price Index. Of greatest concern, perhaps, to a health-conscious society is the recognition that alcoholic beverages contribute $50 per person per year in taxes; yet, the health and social costs are well over $300 per person per year. Only 4% of these taxes are returned for medical services, research or teaching.

Considering our country as a whole, survey data suggest that a third of the adult population consists of abstainers or of persons who seldom take a drink. Another third consists of people who have up to three drinks per week.* The remaining third consumes four or more drinks per week.[3] Because there is likely a dose-response relationship between the amount of alcohol consumed and some of the medical consequences, it is estimated that those consuming the most alcohol will have the greatest medical consequences. The consequences of prolonged and heavy alcohol use in the 15% of the population consuming 75% of the alcohol include excess mortality rates from cirrhosis, accidents, infection and cancer.

Although the history of alcohol intake may be subject to error, Klatsky and co-workers studied ten-year mortality data among four groups of more than 2,000 persons matched for age, sex, race and cigarette smoking.[4] This study depended on classification of the outcome by a death certificate. The cohort for the study was administered a Kaiser Foundation Health Plan questionnaire in which persons were asked two questions about alcohol use: "In the past year did you drink any alcohol? If yes, how many drinks did you usually have?" The options were nine or more per day, six to eight per day, three to five per day or two or fewer per day. The authors matched, by computer, persons reporting a use of more than six drinks to each of three controls: a nondrinker, a person consuming two or fewer drinks and a person taking three to five drinks. The authors studied 97% of all those reporting six or more drinks. They assumed some degree of underreporting of drinking habits, especially among those with heavy alcohol use. The threshold for increased mortality was shown to be in the range of a regular use of three to five drinks; the risk rose sharply at six or more drinks per day.

One may question the accuracy of death certificates as the primary source of mortality statistics. It is also possible with a declining autopsy rate that death certificates may seriously underestimate the prevalence of important diseases. Taylor and colleagues[5] studied the standard autopsy for determining the cause of death and found discrepancies in 40% of cases between findings at autopsy and death certificates. Alcohol-related problems were found in only 36% of death certificates; in contrast, alcohol-related pathology was found in 72% of autopsies. Thus, the use of only death certificates seriously underestimates alcohol-related mortality. Despite the limitations, these data do suggest a threshold of increased mortality related to alcohol in the range of three to five drinks per day.

Immediate Effects

Studying the immediate effects of alcohol on the nervous system provides a reasonable estimate of the risks of alcohol consumption. The response of a person not tolerant to alcohol correlates well with the dose of alcohol administered and the blood alcohol concentration. The neurologic impairments vary with the rate of rise of the alcohol level, prior alcohol exposure, genetic factors, concurrent use of other drugs and absolute dose of alcohol ingested.[6] In a nontolerant person impairment of motor coordination, sensory perception and cognitive function usually occurs at a blood concentration of between 31 and 65 mg per dl.[6] Because alcohol distributes in body water, the resulting concentration will be proportional to body size. Smaller persons will have higher blood concentrations of alcohol than larger persons given the same dose.

Tolerance to alcohol likely occurs at the cellular level. It has been shown that membranes from alcohol-dependent animals resist the acute fluidizing effects of alcohol. It is possible that tolerance may represent cellular adaptation that limits the entry of alcohol into membranes and compensates for the biophysical effects of alcohol within the membranes.[6] Understanding the molecular mechanisms underlying acute intoxication, tolerance and withdrawal may allow for more accurate dose-effects studies.

There are many neurologic diseases associated with the prolonged use of alcohol. Whether the structural neurologic changes associated with this use of alcohol are a result of alcohol toxicity itself or of nutritional deficiencies is unknown. Polyneuropathy, cerebellar degeneration and Wernicke's encephalopathy are common disorders associated with alcohol use. Recent epidemiologic studies have even implicated acute intoxication as a risk factor for ischemic cerebral infarction in young persons.[6] The equivalent of five to six drinks per day is suggested as being related to an increased risk for ischemic cerebral infarction in persons younger than 40 years. It is possible that these changes are

*One drink is estimated to be about 30 ml (1 oz) of 86-proof alcohol containing approximately 10 grams of alcohol.

related to osmolality, changes in coagulation or altered blood pressure. A relationship between heavy alcohol consumption and subarachnoid hemorrhage has also been reported. Although the question of direct effects of alcohol on the cerebral circulation requires further study, variables of cigarette smoking and hypertension are likely contributing factors. It remains possible that alcohol has a direct effect on risk factors for ischemic cerebral infarction and subarachnoid hemorrhage.[6]

Unfortunately, very little is known about the extent of alcohol-related cognitive decrements in the general population or the thresholds for these effects. The availability of computed tomographic (CT) brain scanning and more sophisticated neuropsychometric testing provides new methods to study the problem. Few studies to date adequately control for alcohol consumption, nutritional state or the use of other drugs and they often lack precise methods of assuring abstinence. Even clinically unimpaired drinkers during detoxification may have neuropsychological and CT abnormalities.[7-10] Especially difficult is the quantitative assessment of alcohol's effect in predicting cortical atrophy or cognitive dysfunction. This has made it almost impossible to precisely define the lower limits of these effects. Even if studies of clinically unimpaired persons who consume large amounts of alcohol are carefully controlled for age, there may be subtle differences in CT scanning or neuropsychological testing. Because it is equally difficult to control for nutritional variables and neuropsychological measurements before any alcohol consumption, it is not yet possible to quantitate the lowest dose of alcohol required to injure the nervous system. The evidence for reversibility of CT abnormalities requires further study. Reliable, inexpensive neuropsychological indicators to follow reversibility are needed.

This new information raises important questions of whether or not there are CT abnormalities or neuropsychological deficits that precede the onset of alcohol abuse. Tarter and associates[11] studied neuropsychological deficits in children who are at risk for alcohol abuse. The problems of control variables and bias are immense. By investigating two groups of adolescents who differed only on the basis of the presence or absence of paternal alcohol consumption, suggestive data are presented that neuropsychological impairments that may have been considered to be a consequence of alcohol use may, in some instances, have actually preceded alcohol consumption.[11] Thus, prospective studies of persons at risk is the best research paradigm for answering the threshold question of alcohol toxicity to the nervous system.

Populations at Risk

Alcohol and many other drugs cross the placenta and affect the fetus. What is the threshold for the effect on a fetus? A common pattern of birth defects and mental retardation among some children of women consuming large amounts of alcohol raises serious concern and has prompted intensive research into the relationship between alcohol consumption and pregnancy. French investigators and independent US investigators have identified specific malformations that have been labeled the fetal alcohol syndrome. Children of women who drink heavily may not have all the manifestations of this syndrome but may present with only lowered birth weight or learning deficits. Data on miscarriages, stillbirths and abortions have posed immense scientific difficulties in affirming the dose-response relationships of alcohol consumption and fetal injury. Control of smoking, diet, other drugs and occupational exposures currently frustrates investigators. Most studies to date in animals and humans strongly suggest that alcohol is teratogenic and embryotoxic.[3]

Quellette and colleagues[12] studied heavy drinkers defined as consuming an average of more than 45 ml of absolute alcohol per day, with five or more drinks on at least one occasion per month. After delivery, a detailed evaluation showed that twice as many infants born to heavily drinking mothers were abnormal compared with infants born to either moderately drinking or rarely drinking women. In another study, the offspring of women who consumed 39 ml or more of absolute alcohol per day just before or during pregnancy were compared with those of light drinkers or women who abstained.[13] The evaluations, conducted without prior knowledge of maternal consumption, showed clinical features of abnormal growth and morphogenesis in babies born to heavy drinkers. Other studies attempting to control for smoking have shown that two to six drinking sessions per week at levels as low as 30 ml of absolute alcohol per session or even as low as 15 to 30 ml per day alter the risk of spontaneous abortion.[14]

Other effects during pregnancy, such as the direct pharmacologic effect of alcohol on infant vital function or consumption of alcohol during lactation, require further study. What has emerged from this information is an apparent correlation between maternal alcohol consumption and a risk of fetal abnormalities. Although it has been difficult to control for all variables, drinking alcohol does place a pregnancy at risk; no safe level of maternal alcohol consumption during pregnancy has been defined. Studies of paternal alcohol use in animals and humans and the effect on fetal outcome are also as yet inconclusive.[15]

Of special note is that the desire to have a healthy baby is a powerful motivating force in modifying alcohol consumption. Examination of cohorts of newborns suggests the benefits to offspring when drinking ceases before the third trimester.[16] There may be a critical period in the early weeks after conception when many women are unaware that they are pregnant in which alcohol could pose special problems. Because the lowest threshold of effects has not been defined, some have advocated that if a woman is planning to become pregnant she should give up alcohol altogether or limit herself to less than one drink per day.[17,18]

Pregnant women may be only one of the groups at risk for alcohol effects. Studies of special ethnic groups in which the rate of alcohol metabolism is examined yield statistically significant differences, but there have been few clinical correlates to establish the importance of these metabolic differences. Immediate or prolonged changes of tolerance may also vary with race but, generally, studies in this area have not provided information to allow reliable predictors of populations at risk. It has been suggested that physicians are more vulnerable to alcohol and drug dependency than the general population. Drug use and abuse of prescription drugs may also be more prevalent among physicians, although this is difficult to study, as physicians may come to attention at a higher rate than nonphysicians. Close monitoring of physicians may, in part, account for the better prognosis that is alleged for physicians with alcohol and drug-dependency

problems.[19] Special alcohol problems among seamen, priests and military personnel have also been suggested. Similar difficulties have also been reported for unemployed persons or for those who work changing schedules.[20] Occupational variables are so difficult to control for that all of these studies require more precise methods.

Alcohol and Cancer

The clinical recognition that cancer of the mouth, pharynx, larynx, esophagus and liver appears to have a relationship to alcohol consumption has initiated research into the possible role that alcohol might play in carcinogenesis. In case-control studies an increased incidence of selected types of cancer has been found in a number of different populations throughout the world and these have been related to alcohol consumption. Although the mechanism for this effect is unknown, there have been attempts to control other variables such as smoking, nutrition and hygiene. Because the mechanism by which alcohol might increase the risk of cancer is unknown, it has been difficult in case-control methods to consider all the variables. Pollack and colleagues[21] conducted a prospective cohort study of the relationship between alcohol consumption and the subsequent occurrence of epithelial cancer at five specific sites to determine the impact of alcohol when carefully controlled for age, cigarette smoking and type of alcoholic beverage. The authors found a positive association between monthly alcohol consumption in the range of 15 liters (500 oz) and an increased risk of rectal cancer in Japanese men in Hawaii.

Although the methodologic problems in this type of research are evident, the consistency of findings is impressive. Much more information is required before a threshold level of alcohol consumption as it relates to cancer can be established.[21,22] Alcohol itself does not appear to be a carcinogen in most systems tested, but it is a good solvent for other chemicals and may carry potential carcinogens produced in fermentation or processing.

Gastrointestinal Effects

Alcohol can injure the esophagus, stomach, small intestine, pancreas and liver. Short- and long-term alcohol consumption results in direct injury to the mucosa of the upper gastrointestinal tract. The mechanism of this injury and the dose of alcohol required are unclear. Even small doses of alcohol can directly or indirectly stimulate acid secretion or cause alteration of the mucous protective barrier of the upper gastrointestinal tract. Oral and intravenous administration of alcohol, even in relatively small doses, may cause alterations in gastrointestinal motility and alter absorption of essential nutrients.[3] Alcohol increases pancreatic secretion and may cause obstruction to pancreatic secretions, resulting in increased pancreatic pressure and extravasation of pancreatic secretions into interstitial tissues, thus injuring the pancreas.

Bjarnason and co-workers[23] studied intestinal permeability with sodium chromate[51] Cr-labeled ethylenediaminetetraacetic acid in nonintoxicated patients who had alcoholism but without cirrhosis or overt clinical manifestations of malabsorption or malnutrition. These patients consumed about five to ten drinks of alcohol per day for three years and showed an increase in intestinal permeability to compounds with a molecular weight less than 5,000. Although this method does not indicate the exact site of the altered permeability, the overall abnormalities of absorption suggest that even in the absence of obvious malabsorption, increased permeability could accelerate intestinal damage by the loss of essential nutrients. Unfortunately, it is not known at this time whether lower doses of alcohol will also cause this abnormality of gastrointestinal absorption.

Even though persons who drink alcohol regularly may apparently consume a normal number of calories, they are malnourished by the standards of appropriate laboratory tests. One gram of alcohol supplies 7.1 calories and a liter of spirits produces about 3,300 calories. Because alcohol cannot be stored, it must be metabolized and the calories derived make no contribution to the energy of nutrition but may contribute to obesity. There are many reasons, in addition to the intestinal leak described, why persons with chronic alcoholism might become malnourished. These reasons have been fully reviewed recently by Sherlock.[24] Obviously, there can be end-organ damage to the upper gastrointestinal tract, pancreas or liver. Alcohol causes alterations of protein synthesis and amino acid metabolism and may alter important immune mechanisms, mineral and electrolyte balances and vitamin absorption and utilization. Unfortunately, the exact dose of alcohol that increases the minimum daily requirements of essential nutrients, or the exact dose that would cause end-organ damage, is not known. Until the basic mechanism for these toxicities is understood, a rational recommendation as to the minimum dose to ensure safety cannot be given.

Alcohol consumption is also associated with hyperuricemia and gout. With prolonged administration of alcohol to gouty patients with normal renal function, a mean peak blood alcohol concentration of only 13 mg per dl was shown to increase urate synthesis by enhancing the turnover of adenine nucleotides.[25] Higher blood concentrations of alcohol or lactate (or both) may alter urate clearances but only at much higher blood alcohol levels. Because hyperuricemia is recognized as a possible biochemical marker for alcohol ingestion and there is a higher incidence of gout among regular drinkers, these changes in nucleotide metabolism may have important consequences in identifying markers of alcohol intake as well as pathologic mechanisms.

The nutritional deficiencies of water-soluble vitamins and the threshold for their induction by alcohol are now recognized to be subtle. Although classic thiamine deficiency and Wernicke's encephalopathy resulting from thiamine deficiency are still prevalent, much more subtle nutritional deficiencies are likely to be present.

Recent studies conducted in humans and in animals show that prolonged consumption of alcohol even associated with an adequate diet may result in a striking lowering of hepatic fat-soluble vitamins, especially vitamin A. Even Mallory's bodies in the liver, long associated with excess alcohol consumption, are postulated to be lesions that may result from vitamin A deficiency.[26] Because large supplements of vitamin A are known to be hepatotoxic, much more must be learned concerning doses of alcohol and their effect on vitamin A. It is possible that the toxicity of vitamin A is not due to vitamin A itself but rather to one of its metabolites because the theoretical beneficial effect of vitamin A supplementation falls within a very narrow range. Many more studies are required

before therapeutic recommendations for vitamin A replacement therapy are justified.[26,27]

The liver is one of the key organs of metabolism of alcohol and is relatively easily deranged with prolonged consumption. Because the mechanism by which alcohol causes fatty liver, alcoholic hepatitis or cirrhosis is not currently known, it is difficult to estimate the total dose required to produce these pathologic changes. Suggestions from France are that as little as 60 grams a day (about six drinks) will suffice to cause liver dysfunction in men and as little as 20 grams a day (about two drinks) in women.[28] Acetaldehyde and superoxide anion have been suggested to be mediators for the more advanced features of alcohol-induced liver dysfunction.[29] Because the liver is so essential in the detoxification of many substances, it is also theoretically possible that alcohol alters basic liver function and that other toxic agents are the primary cause of the liver disease. Immunologic abnormalities have also recently been described to account for alcohol-induced liver disease.[30] Of special note are sex-related differences in cases of alcohol-induced liver disease.[31,32] Changes induced by estrogens or alterations of peak blood concentrations of alcohol in women have suggested—but do not prove—the observed sex differences in the susceptibility to alcohol-induced liver damage. Nonetheless, these pose important indices that must be added to any assessment of risk for alcohol consumption.

It has been suggested that persons who are symptomless carriers of the hepatitis B surface antigen (HBsAg) are at risk for alcohol-induced liver abnormalities. An amount of alcohol that is harmless to HBsAg-negative subjects, 80 grams (about eight glasses) of wine appears to enhance liver damage.[33] Unfortunately, there were not enough women in the study to test the susceptibility of the hepatotoxic effects of alcohol in HBsAg-positive female carriers.

Cardiovascular Effects

Alcohol administration alters the cardiovascular system in many ways. Direct injury to the myocardium from alcohol or one of its metabolites was initially thought to be due to thiamine deficiency or contaminants in alcoholic beverages. Alcohol cardiomyopathy is now thought to occur in men with heavy drinking episodes over a prolonged period and is not solely due to thiamine deficiency. Arrhythmias associated with social drinking or alcohol withdrawal have also been described in studies, such effects being labeled "holiday heart."[34,35] After the administration of 90 ml of 80-proof alcohol, significant atrial or ventricular arrhythmias developed in 10 of 14 patients. It is possible that these changes are due to direct effects of alcohol or to alterations of electrolyte balance.

Alcohol use is also apparently linearly related to systolic and diastolic blood pressure independent of adiposity, salt intake, coffee drinking or cigarette smoking.[36,37] Although magnesium deficiency has also been associated with changes in blood pressure and alcohol intake, convincing data are not yet available to link these two observations. Current data do not show the threshold of alcohol administration that causes alterations in electrolyte balance. The alcohol-related increase in blood pressure is likely an important clinical factor when diagnosing and treating hypertension.

The incidence of coronary heart disease has been suggested to be lower in persons consuming less than three drinks per day when compared with persons who totally abstain from alcohol. The notion that small amounts of alcohol consumption might be protective to the cardiovascular system emerged from evidence suggesting that elevated levels of circulating high-density lipoprotein (HDL) occur with alcohol consumption. However, more recent studies note that HDL is a heterogeneous group of lipoproteins with at least two major subclasses.[38,39] The less dense HDL_2 is epidemiologically associated with reduction of heart disease risk and the more dense HDL_3 is not clearly related to heart disease. Exercise and estrogens increase HDL_2, not HDL_3. Haskel and colleagues[38] showed that administration of one to three drinks of alcohol per day raised levels of HDL_3 but not HDL_2. When this quantity of alcohol was stopped, levels of HDL_3, not HDL_2, decreased. The complexity of these observations has been summarized by Lieber.[39] Epidemiologic studies do suggest, when carefully controlled, that modest alcohol intake is associated with a decreased incidence of coronary heart disease and with increased levels of HDL_3, rather than HDL_2. In the absence of severe liver disease, high alcohol intake results in high levels of HDL_2, but there is no evidence of protection against coronary heart disease. When alcohol use is associated with severe liver disease, HDL fractions decrease. The clinical significance of this information is not fully appreciated as yet.

Endocrine Effects

In the past ten years a substantial amount of literature has been produced on the effect of alcohol on the endocrine system.[40] Sex-related differences in the hypothalamic pituitary gonadal axis, alterations of steroidogenic enzymes and altered hormone binding have all been described. Symptoms of altered endocrine function, especially in men with liver disease, are well known. Gynecomastia, loss of hair, testicular atrophy and spider angiomata may be effects of alcoholic or liver disease or both. Whether these changes occur without liver dysfunction is an unresolved question that requires further study.

Alcohol and Aging

West and associates have reviewed the significant medical, psychiatric and social implications of alcohol consumption in the elderly.[1] Alcohol use is the second leading cause of admission of elderly persons to psychiatric institutions. Elderly persons do have altered pharmacokinetics for alcohol; the volume of distribution of alcohol is lower in the elderly, yet plasma clearance rates are unchanged. In addition, older persons seem to have greater brain sensitivity to alcohol than younger. Pharmacokinetic factors do not account for the greater vulnerability of normal elderly persons to alcohol. Although it is claimed that small amounts of alcohol may be useful therapeutically for elderly persons, current information does not tell us the threshold for safety in aging patients.

Alcohol Chemical-Drug Interactions

Many studies have shown the important pharmacologic and therapeutic interactions of alcohol with many drugs and chemicals. Alcohol may occasionally antagonize other drug effects, but most often it is additive or superadditive. Because it is a potent enzyme inducer, alcohol may appear to antago-

nize the effects of other agents until abnormalities of liver function occur.

Commonly, alcohol acts directly as a sedative hypnotic agent working at a similar site of action with other sedative hypnotic agents. Alcohol may indirectly alter absorption, distribution, excretion or metabolism of other agents. Potentially serious interactions between alcohol and chemical agents in the workplace exist. Amides, oximes, thiurams and carbamates are all known to inhibit the enzyme aldehyde dehydrogenase.[41] These agents produce symptoms similar to those seen with elevated acetaldehyde levels that result after disulfiram (Antabuse) is mixed with alcohol. Alcohol is also known to enhance the toxicity of many halogenated hydrocarbons, especially carbon tetrachloride and trichloroethylene. Because even small amounts of alcohol can cause these interactions, workplace exposures must be added to the risk analysis of alcohol use.

An especially important type of alcohol interaction occurs with over-the-counter products, particularly aspirin. Ingesting less than 50 grams (about five drinks) of alcohol prolongs the bleeding time of normal subjects receiving as little as 325 mg of aspirin.[42] Alcohol has no demonstrable effect on bleeding time. When aspirin and alcohol are mixed, there will be pronounced prolongation of bleeding for at least 36 hours.[42] One must be careful to weigh this type of interaction when making an overall health risk assessment. A 50-gram dose of alcohol (approximately five drinks) is associated with the alcohol concentrations that are often achieved in social settings.

Drug Abuse

Inhalants, hallucinogens, cocaine, abuse of prescription psychotherapeutic agents and marijuana are the most widely used nontherapeutic psychoactive drugs. Emergency management of intoxication, overdose and withdrawal syndromes is now widely recognized as a common continuing medical problem.[43] Nicholi[44] has reviewed the current widespread use of nontherapeutic psychoactive agents, which he calls a "modern epidemic." Drug abuse survey data presented in many studies are limited because of lack of supporting toxicology laboratory data, poor documentation for drug interactions, lack of quantitative dose estimations and confounding variables of socioeconomic status. Because alcohol is the common background for much of the nontherapeutic use of psychoactive agents, the entire field should be described more appropriately as polydrug abuse. Whether these agents are used for pleasure seeking or for release of discomfort or out of curiosity has never been fully quantitated. The major issue to consider is whether medical sequelae can result from the use of these agents in doses small enough not to impair performance.

There is clear evidence that inhaling glues, coolants, paint thinners, nail polish, gasoline and nitrates can cause major acute and chronic medical consequences. In addition, the use of hallucinogenic agents such as phencyclidine hydrochloride, even in low doses, can be associated with severe medical consequences. Cocaine abuse is apparently spreading throughout the United States. An increase in cocaine "free-base" smoking is likely to increase the number of cocaine users needing medical attention.[45] "Free base" is made by extracting cocaine hydrochloride with alkali; the residue, unlike the hydrochloride, is volatile and not degraded by smoke or heat. Nonpsychiatric complications of chronic cocaine use depend on the route of administration. Nasal septal necrosis with intranasal use, lung damage in smokers and life-threatening infection from intravenous injection[45] can all occur.

Abuse of sedatives or stimulants with or without medical prescriptions is a well-known problem. Because of the difficulty of quantitating the nature of the problem and estimating the total dose delivered, scientists are left with attempts to quantify doses that produce psychological dependency, tolerance and withdrawal.

Based on questionnaire information, marijuana is considered to be the most widely used illicit drug. The health effects of prolonged marijuana use have been extensively reviewed.[44] There is a suggestion that the regular use of marijuana is associated with the use of other psychoactive agents. If parents smoke, drink or use psychoactive agents, their offspring will generally be more prone to use illicit drugs.[44] This area is very complex and is often complicated by a background of alcohol use; there is little scientific evidence to assure that the regular use of nontherapeutic psychoactive agents can in any way be described as safe.

Summary

The analysis of low-dose effects of alcohol and nontherapeutic psychoactive drugs is bewilderingly complicated because we do not know the basic mechanism of injury for these agents. Clinical diagnostic tests are often imprecise in separating tissue effect from tissue pathology. The risk assessment of low doses of these agents has inherent limitations. Basic weaknesses in epidemiology, animal extrapolations and interactions heighten the difficulty. What risk is "acceptable" to the individual or society? Freedom of individual choice may conflict with public policy. There is also the reality of the impossibility of complete removal of risk.

Unfortunately, risk assessment must proceed with incomplete information if we are to give rational personal health promotion recommendations.[46] This poses an enlightened challenge that must be addressed with insufficient information. Given the information at hand the following are reasonable suggestions for personal health maintenance:

- Illicit recreational drug use of inhalants, hallucinogens, stimulants, narcotics and sedative hypnotic drugs poses an unacceptable risk.
- Groups at special risk, such as persons who have been alcohol or drug abusers, pregnant patients, elderly persons or patients taking other medications including aspirin should not ingest alcohol or other medications unless they are under medical supervision.
- The threshold for increased mortality from "regular" use of alcohol is three to five drinks; the risk rises sharply after six or more drinks per day. Cardiovascular mortality data concerning one to two drinks per day compared with total abstention suggest a favorable outcome, but further studies are required.
- Current advertising, availability and cost factors for alcohol require modification for optimal health maintenance. Insufficient financial resources are presently devoted to education, patient services and research.

Recognizing the shortcomings of the information base on which these recommendations are made, it is clear that with

insufficient dollars for health care, it will be necessary to redefine these recommendations for individuals and society as more is learned.

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